1952

Formulation of an improved ointment base

Leonard James Barnes
The University of Montana

FORMULATION OF AN IMPROVED OINTMENT BASE

by

LEONARD JAMES BARNES
B.S., Montana State University, 1949

Presented in partial fulfillment
of the requirements for the degree of
Master of Science

Montana State University
1952

This thesis has been approved by the Board of Examiners in partial fulfillment of the requirements for the degree of Master of Science.

Chairman of the Board of Examiners

Dean of the Graduate School

Date June 7 1952

ACKNOWLEDGMENTS

The author herewith gratefully recognizes the generous aid and guidance of Dr. John F. Suchy and the helpful suggestions of Dr. Witold Saski, in the successful completion of this work, and to Mrs. L. J. Barnes for assistance in preparing the manuscript.

L.J.B.

TABLE OF CONTENTS

LIST OF TABLES

CHAPTER I

INTRODUCTION

Only recently has pharmaceutical research entered the field of water soluble ointment bases. Much has been done and much still remains to be done in attaining the "ideal" ointment base.

Included under Water Soluble Ointment Bases in Remington's "Practice of Pharmacy", are "those which are prepared from the higher Ethylene Glycol polymers known as Carbowax Compounds". In this work the semi-solid preparations produced through the use of bentonite, colloidal magnesium aluminum silicate, gelatin, pectin, sodium alginate, or silica gel are included.

During the entire course of development, the properties of an ideal ointment base were constantly kept in mind. Of the following "ideal" list, the first eleven are included in Remington's "Practice of Pharmacy".

1. Pharmaceutical elegance.
2. A low index of irritation.
3. Non-dehydrating properties.
4. Non-greasy properties.
5. A neutral reaction.
6. Good keeping qualities.
7. Compatibility with common medicaments.

8. Ability to efficiently release medicaments at the site of application.

9. Washability (easy removal with water).

10. A minimum number of ingredients.

11. Ease of compounding.

In addition an ideal ointment base should possess:

12. Non-sensitizing action.

13. Versatility for extemporaneous compounding.

14. Hydrophilic properties.

15. Water retainability.

Furthermore, such a base should be economical in cost, (ingredients and compounding).

CHAPTER II

THEORETICAL

Pectin, N.F. was chosen as an ingredient in the proposed ointment base because of its properties in Pectin Paste, N.F. This preparation, although water soluble, takes up large quantities of water and yet retains it's consistency. It is slightly acidic in nature, a desirable property in an ointment base, for the normal skin has an "acid mantle" with a pH of 4.2 to 5.6 with an average ranging between 5.3 and 5.6. This acidic condition apparently imparts bactericidal properties.[1]

It has been shown that skins which are unable to neutralize alkaline soap solutions are more prone to sensitization.[2] In diseased skin areas, the pH is often disrupted to the point where it becomes alkaline.

This acidity may be a healing factor, or it may possess the ability to form a protective coating capable of maintaining a high water content, properties utilized in the economical and successful treatment of resistant bed sores and ulcers at the Cook County Hospital.[3] At this project, it was also pointed out that this paste may serve as a culture medium for exposed tissue.

---

1. The pH of Ointments; Pract. Edit. J. A.Ph.A.; Vol. 3; Pg. 340; Oct. 1942.

2. Ibid.

3. Bernard Fantus and H. A. Dyniewicz; Pastes 1. For Dermatologic Use; J. A.Ph.A.; Vol. 28; Pg. 548; Aug. 1942.

When Pectin Paste, N.F. is exposed to air, it forms a tough collodion-like film. This serves to retain underlying moisture.

The Pectin Paste formula in the N.F. (9th Edition), is:

Pectin	75 Gms.
Glycerin	180 Gms.
Benzoic Acid	2 Gms.
Ringer's Sol. # 1 q.s. To make about	1000 Gms.

The above is easily compounded by dissolving the Benzoic Acid in 825 c.c. Ringer's Solution #1, heated to 100°C. and adding this solution, with stirring, to the Pectin thoroughly "wetted" with the glycerin, (using a dry container) and stirring until an homogenous mass is formed.

The incorporation of 7.5 percent Pectin forms a paste of a consistency which has little flow, but which still possesses a tenacious, adhering quality, with the ability to form an even surface film.

The Glycerin serves to "wet" the pectin particles and due to its hygroscopic nature improves the water-retaining property of the preparation.

The Benzoic Acid acts as a preservative. Without it, Pectin Paste is subject to bacterial and mould growths.

Ringer's solution not only gives the paste a balanced isotonic content, but causes the pH to approach neutrality. (approximately pH 4.5 to pH 5.5).[1]

The paste is inexpensive, consisting mostly of water, with small amounts of low cost ingredients. The compounding technique is simple.

As an ointment, Pectin Paste, N.F. possesses little pharmaceutical elegance. It lacks the appearance, the texture, and the qualities of actual application such as feel, consistency, or "slip".

Pectin Paste, N.F. because of its low irritability, is a desirable base for ointments used in the treatment of external raw areas. Stearyl Alcohol, which has been widely used to give consistency to ointments, may also be used readily in Pectin Paste, N.F.

Ointments prepared from pectin naturally have a high water content, and as such, tend to be non-dehydrating.

Greasiness, an undesirable property in ointments, is eliminated by the use of pectin. In fact, Stearyl Alcohol is added often to such ointments to give a better "greasy feel".

Pectin Paste, N.F. is incompatible with alkalies,[2] which is to be expected since pectin is composed mostly of Col-

---

1. W. D. Maclay, Alland Shepherd & Harry Lotzkar; Use of Pectin in Pharmaceutical Pastes and Ointments; Scient. Ed. J. A.Ph.A., Vol 33; Pg. 113-118; April 1944.

2. Goldner, Karl J.; Pectin Emulsions and Ointments; Pract. Ed. J. A.Ph.A., Vol. 13; Pg. 324-26; Sept. 1942.

loidal Polygalacturonic Acids.[1] Incompatibilities from this source may, however, be remedied by buffering.

Pectin, as a gel or paste, is very prone to mould growths. The N.F. paste contains 0.2 percent of Benzoic Acid added as a preservative to increase shelf life by inhibiting mould growths. Methyl and Propyl Paraben have both been used successfully as preservatives in U.S.P. Hydrophilic Ointment. Zephiran Chloride (officially, Benzalkonium Chloride, U.S.P.) has found application in biologicals and in ointment bases.[2,3]

Previous workers have found that pectin is compatible with a wide range of medicaments.[4,5] Efficient release of medicaments at the site of application has also been shown experimentally.

The initial preparation, Pectin Paste, N.F. is soluble and leaves no stain. Stearyl Alcohol is used in Modified Landon-Zopf Base and Canadian Formulary Base, both of which are

---

1. Kertesz, Z. I.; The Pectinic Substances; Interscience Publishers, Inc.; New York; Pg. 5; 1951.

2. Eugene Maier (Venice Florida); Preservation of Biological Fluids with Alkyl-Dimethyl Benzyl Ammonium Chloride; J. Bacteriology 38; Pg. 33; 1939; July-Dec.

3. Editors; Universal Hydrophilic Ointment Base; J. A.Ph.A.; Pract. Ed; Pg. 475; 1951.

4. W. D. Maclay, Alland Shepherd & Harry Lotzkar, et. al.; Use of Pectin in Pharmaceutical Pastes and Ointments.

5. Karl J. Goldner; Medical and Pharmaceutical Applications of Pectin; Am. J. of Pharmacy; Vol. 114; Pg. 41-6.

characterized as water soluble in Remington's "Practice of Pharmacy". Stearyl Alcohol was, therefore, made an ingredient in the submitted formula. As for the number of ingredients and ease of compounding, the submitted base compares favorably with Hydrophilic Ointment, U.S.P. or Polyethylene Glycol Ointment, U.S.P.

Extemporaneous compounding of the new base should embrace the direct incorporation of the desired ingredients directly using levigation with an appropriate spatula and ointment slab. If a diluent is necessary, the one most commonly used in similar cases is water. If excessive alkalinity is imminent, Gifford's Acid Buffer Solution with the pH 5 may be used as diluent.

Although pectin acts as an emulsifying agent in compounding, if used alone, it is not satisfactory.[1] The addition of 1.13 percent Polysorbate 80, U.S.P. increases the ability of the ointment to take up oils, etc.

Water-absorbability and water-retainability, were two additional objectives sought in the development of the desired formula.

Both of these objectives were also attained by adding pectin.

---

1. Karl J. Goldner; et. al.; Medical and Pharmaceutical Applications of Pectin.

CHAPTER III

EXPERIMENTAL

FIRST SERIES OF TRIAL BASES

The submitted formula was developed after compounding four series of bases. Each series of bases was evaluated and improved until the submitted formula was derived. The first series of bases and pertinent data follow.

BASE I:

Methyl Cellulose, (25 cps.)	7.5 Gm.
Sodium Alginate	1.0 Gm.
Distilled Water	51.0 c.c.

Heat water to 90°C. Add the Sodium Alginate and Cellulose and allow to macerate for 20 minutes. Cool and stir until homogenous.

BASE 2:

Pectin	7.5 Gm.
Sodium Alginate	1.0 Gm.
Glycerin	18.0 Gm.
Water or (Ringer's Sol. #1)	74.0 c.c.

Heat the Ringer's solution to 100°C. and add to the Sodium Alginate and Pectin that has been thoroughly "wetted" by the Glycerin. Stir until a paste forms.

BASE 3:

Methyl Cellulose (100 cps.)	10 Gm.
Distilled Water	90 c.c.

Heat 45 c.c. of the water to 90°C., add the Cellulose and macerate 20 minutes. Then add the remainder of the water, cool and stir until homogenous.

BASE 4:

Methyl Cellulose (400 cps.)	10 Gm.
Distilled Water	90 c.c.

Heat 45 c.c. of the water to 90°C. Add the Cellulose, macerate 20 minutes, then add the rest of the water, cool and stir until homogenous.

Upon adding equal parts of Base 1 and of Pectin Paste, N.F. and levigating, a product of ointment-like consistency resulted which had the ability to absorb large quantities of water. The appearance of the product was otherwise similar to that of Pectin Paste, N.F.

Equal parts of Base 2 and Base 4 yielded a compatible product the consistnecy of which was, however, poor.

The cellulose preparations (Bases 1, 3 and 4) also had ointment-like consistency, but were opaque, jelly-like, stiff and sticky.

Stearyl Alcohol was next added to Bases 5 and 6 to improve appearance.

BASE 5:

Pectin	7.5 Gm.
Glycerin	18.0 Gm.
Sodium Alginate	.5 Gm.
Stearyl Alcohol	3.0 Gm.
Distilled Water	71.0 c.c.

Dissolve the Sodium Alginate in the water and bring to boiling. Add this to the mixture of pectin, well coated with glycerin, and the alcohol. Stir while cooling until a smooth base results.

BASE 6:

Pectin	7.0 Gm.
Glycerin	18.0 Gm.
Stearyl Alcohol	5.0 Gm.
Sodium Lauryl Sulfate	0.5 Gm.
Distilled Water	69.5 c.c.

Procedure as under Base 5, except that Sodium Lauryl Sulfate was substituted for the Alginate.

The products which resulted from the compounding of Bases 5 and 6 were smooth ointment-like preparations with good application qualities. Both adhered well and washed off easily. Addition of 50 percent of water to each resulted in a heavy creamy product of excellent consistency.

SECOND SERIES OF TRIAL BASES

The next eight bases were compounded by modifying the formulas of Bases 5 and 6 using Methyl Cellulose, Pectin, Sodium Alginate, Glycerin, Stearyl Alcohol and a surface-active agent.

All of these bases were tested for water-absorbability and water-retainability, with the purpose of determining what combination would possess these properties in the highest degree. The following combinations make up the second series of bases investigated.

BASE 7:

Pectin	7 Gm.
Glycerin	18 Gm.
Stearyl Alcohol	7 Gm.
Sodium Lauryl Sulfate	.5 Gm.
Water	67.5 c.c.

BASE 8:

Pectin	6.0 Gm.
Methyl Cellulose (cps. 25)	6.0 Gm.
Glycerin	18.0 Gm.
Stearyl Alcohol	6.0 Gm.
Sodium Lauryl Sulfate	.5 Gm.
Water	63.5 c.c.

BASE 9:

Pectin	7.0 Gm.
Glycerin	20.0 Gm.
Sodium Alginate	3.0 Gm.
Sodium Lauryl Sulfate	.7 Gm.
Calcium Gluconate	.3 Gm.
Stearyl Alcohol	5.0 Gm.
Water	64.0 c.c.

BASE 10:

Pectin	5.0 Gm.
Sodium Alginate	2.0 Gm.
Methyl Cellulose (15 cps.)	5.0 Gm.
Glycerin	20.0 Gm.
Calcium Gluconate	.2 Gm.
Distilled Water	67.8 c.c.

BASE 11:

Pectin	6.0 Gm.
Sodium Alginate	2.0 Gm.
Polysorbate 80	1.0 c.c.
Stearyl Alcohol	5.0 Gm.
Glycerin	15.0 Gm.
Distilled Water	71 c.c.

BASE 12:

Pectin	5.0 Gm.
Sodium Alginate	1.0 Gm.
Methyl Cellulose (15 cps.)	3.0 Gm.
Glycerin	18.0 Gm.
Polysorbate 80	1.0 c.c.
Stearyl Alcohol	4.0 Gm.
Distilled Water	68.0 c.c.

BASE 13:

Pectin	7.0 Gm.
Glycerin	18.0 Gm.
Stearyl Alcohol	7.0 Gm.
Polysorbate 80	2.0 c.c.
Distilled Water	66.0 c.c.

BASE 14:

Pectin	6.0 Gm.
Sodium Alginate	1.0 Gm.
Methyl Cellulose (15 cps.)	3.0 Gm.
Glycerin	18.0 Gm.
Calcium Gluconate	.1 Gm.
Polysorbate 80	1.9 c.c.
Distilled Water	70.0 c.c

The soluble ingredients of Bases 7 to 14 were dissolved in the water with the aid of heat. The alcohol was added and the mixture brought to boiling. The resulting solution was then added all at once to the well-wetted pectin-glycerin mixture and the whole was stirred vigorously until a gel was formed.

The stirring was continued until a final homogenous preparation resulted. Special care was accorded to the cellulose preparations by allowing the cellulose to macerate in the water solution at 90°C. for 15-20 minutes prior to adding the alcohol and heating to boiling.

Calcium Gluconate was added in the hope of improving consistency.

Polysorbate 80, a surface-active agent, was added with a twofold purpose, (1) it is an excellent emulsifier, (2) and improves the dispersing qualities of bases in compounding. It is soluble in water and can be easily measured.

It was found, while compounding Bases 7 to 14, that unless a certain procedure was followed, the initial gel would contain lumps of unmixed pectin which could not be stirred to smoothness. This incompatibility was apparently caused by the product's cooling too rapidly when the alcohol was included in the pectin mixture.

Bases 7 to 14 were stored at room temperature in ointment jars. A rough evaporation test was performed by weighing 20 Grams of each on a prescription balance, removing to an ointment slab and incorporating into each 10 c.c. of distilled water, measured by a pipette. Each sample thus prepared was then placed on a watch glass and allowed to evaporate for exactly nine hours and re-weighed. The results are shown in Table I.

In a control test, 20 Gram samples of each base were taken and treated as above, no water being added. Care was taken in both series of tests to obtain, as nearly as possible, the losses in weight. The results are also shown in Table I. Although great care was exercised in transfering the ingredients to the slab, a small margin of error necessarily could not be avoided.

The sodium alginate combination results indicated excellent water-retainability, a fact corroborated by the twenty-four hour plain-base control evaporation test. The pectin-alcohol combinations showed good water-retainability in the nine hour test, but in the plain-base evaporation test, the results proved not too satisfactory.

The cellulose combinations, on the other hand, possessed little water-retainability and the results led to discontinuation of its use in this work.

TABLE I:

COMPARISON OF PERCENT WATER LOSS FROM BASES AFTER NINE AND TWENTY-FOUR HOUR EVAPORATION INTERVALS

Combination	Base	Water Addition Base Loss after 9 hours	Plain Base Loss after 24 hours
Sodium Alginate	9	47.8	53.1
Sodium Alginate	11	51.2	57.1
Pectin, Alcohol	7	48.5	77.0
Pectin, Alcohol	13	49.5	72.7
Cellulose, Alginate, Alcohol, Pectin	12	53.8	76.7
Cellulose, Alginate, Pectin	14	57.5	75.7
Cellulose, Alcohol, Pectin	8	60.5	57.8
Cellulose, Alginate, Pectin	10	60.5	66.1
AVERAGE LOSS		53.5	67.0

THIRD SERIES OF TRIAL BASES

A third series of four bases patterned after the more desirable sodium alginate combinations of the preceding series was next compounded. The pectin, stearyl alcohol and sodium alginate content of this group of bases was varied to determine the most satisfactory proportions of these substances.

BASE 15:

Pectin	7.0 Gm.
Sodium Alginate	2.0 Gm.
Polysorbate 80	1.0 c.c.
Stearyl Alcohol	5.0 Gm.
Glycerin	20.0 Gm.
Water or (Ringer's Sol. #1)	65.0 c.c.
To make about	100.0 Gm.

BASE 16:

Pectin	6.0 Gm.
Sodium Alginate	3.0 Gm.
Duponal	0.7 Gm.
Stearyl Alcohol	6.0 Gm.
Calcium Gluconate	.3 Gm.
Glycerin	20.0 Gm.
Distilled Water	64.0 c.c.
To make about	100.0 Gm.

BASE 17:

Pectin	4.0 Gm.
Sodium Alginate	4.0 Gm.
Polysorbate 80	1.0 c.c.
Stearyl Alcohol	6.0 Gm.
Glycerin	18.0 Gm.
Distilled Water	67.0 c.c.
To make about	100.0 Gms.

BASE 18:

Pectin	3.0 Gm.
Sodium Alginate	5.0 Gm.
Polysorbate 80	0.5 c.c.
Stearyl Alcohol	7.0 Gm.
Calcium Gluconate	0.5 Gm.
Glycerin	18.0 Gm.
Distilled Water	66.0 c.c.
To make about	100.0 Gms.

Bases 15 to 18 were compounded by use of the previously described procedure employed in making bases 7 to 14.

A water absorption-retainability test was performed on bases 15 to 18. Hydrophilic Ointment U.S.P., Pectin Paste N.F. and Bases 9 and 11 were used as controls.

Accordingly, 30 Gram samples of each were weighed in 50 c.c. beakers, each tared with a small glass stirring rod. Immediately after weighing, 15 c.c. of distilled water was stirred into each sample. The mixtures were then allowed to evaporate at room temperature and re-weighed after continuous exposure at intervals of 42.5 hours, 66.5 hours, 5 days and 7 days.

The per cent loss of water in each case was calculated, disregarding the small amount of water contained in Polysorbate 80. The results are recorded in Table II.

Identical procedures were used in evaporating 20 Gram samples of each base without the addition of the water. The weighings were made at 44 hour, 68 hour, 5 day and 7 day intervals and the losses of weight similarly calculated. The results are included in Table III.

A study of all of the results thus far obtained revealed that Base 15 had the best water absorption-retainability and that it was followed in this respect by Base 11. The official Hydrophilic Ointment and Pectin Paste were both surpassed in this respect by all of the trial bases.

Relative losses of water from the undiluted Bases 9, 11 and 15 did not exceed 3.5 per cent. Pectin Paste showed a moderate initial loss, but the lowest final loss of the group. Such a loss of water as time progressed was also noted in Base 15.

TABLE II

COMPARISON OF WATER LOSS OF WATER REINFORCED BASES 15 to 18 WITH PECTIN PASTE, N.F., HYDROPHILIC OINTMENT, U.S.P. AND BASES 9 AND 11

Preparation	Percent water loss after evaporation 42.5 hrs.	66.5 hrs.	5 days	7 days
Base 15	10.2	17.9	28.2	36.7
" 11	10.7	18.4	30.1	41.2
" 16	12.4	20.6	31.9	40.9
" 17	11.0	18.7	31.4	43.5
" 9	11.9	20.8	33.9	44.9
Pectin Paste N.F.	12.5	21	34.7	49.2
Base 18	11.7	21	35.4	49.3
Hydrophilic Ointment U.S.P.	17.5	27.3	40.9	53.6

TABLE III

COMPARISON OF PLAIN BASES 15 to 18 WITH PECTIN PASTE, N.F. HYDROPHILIC OINTMENT, U.S.P. AND BASES 9 AND 11

Preparation	Percent water loss after evaporation 44 hrs.	68 hrs.	5 days	7 days
Hydrophilic Ointment, U.S.P.	35.2	47.7	59.9	70.5
Base 9	27.2	38.9	58.5	73.5
" 11	27.9	40.7	61	74.2
" 15	29.0	41.6	61.5	75.2
" 17	29.2	41.8	61.4	75.7
" 16	30.2	42.5	62.7	78.3
" 18	30.1	43.3	64.4	80.5
Pectin Paste, N.F.	27.9	42.0	66.7	83.4

Although Base 15 was selected as the one having the best water-absorbing and retaining properties, its' appearance, texture, feel and "slip" were not those desirable in an "ideal" base.

FOURTH SERIES OF TRIAL BASES

Another series of Bases (19 to 26) was then compounded, using higher percentages of Stearyl Alcohol, with the object of improving appearance, feel and texture.

Preservatives were now added to all of the bases, Methyl and Propyl Paraben being added to Base 22 in the same quantities as are contained in Hydrophilic Ointment, U.S.P.

Proportionate quantities of the parabens as used in official Hydrophilic Ointment were computed and incorporated into Bases 19 and 25. An excess of the preservatives was added to Base 26.

Benzoic Acid, 0.2 percent, was used in Base 20 and Benzalkonium Chloride in Bases 21, 23 and 24, in amounts found successful in a work described in an article in the Journal of the American Pharmaceutical Association.[1]

---

1. Editors; J. A.Ph.A.; Page 475; 1951.

BASE 19:

Pectin	7.0	Gm.
Sodium Alginate	2.0	Gm.
Polysorbate 80	1.0	c.c.
Stearyl Alcohol	5.0	Gm.
Glycerin	20.0	Gm.
Methyl Paraben	.045	Gm.
Propyl Paraben	.027	Gm.
Water or (Ringer's Sol. #1)	65.0	c.c.
To make about	100.0	Gm.

BASE 20:

Pectin	7.0	Gm.
Polysorbate 80	1.0	c.c.
Benzoic Acid	.2	Gm.
Stearyl Alcohol	11.0	Gm.
Glycerin	18.8	Gm.
Water or (Ringer's Sol. #1)	62.0	c.c.
To make about	100.0	Gm.

BASE 21:

Pectin	6.0	Gm.
Polysorbate 80	1.0	c.c.
* Benzalkonium Chloride	.06	c.c.
Stearyl Alcohol	10.0	Gm.
Glycerin	17.94	Gm.
Distilled Water	65.0	c.c.
To make about	100.00	Gm.

BASE 22:

Pectin	6.7	Gm.
Polysorbate 80	1.0	c.c.
Methyl Paraben	.025	Gm.
Propyl Paraben	.015	Gm.
Sodium Alginate	.3	Gm.
Stearyl Alcohol	11.0	Gm.
Glycerin	18.96	Gm.
Distilled Water	62.0	c.c.
To make about	100.00	Gm.

* Zephiran Chloride Concentrate, Aqueous Solution 12.8%, Winthrop-Stearns, used in Bases 21, 23 and 24.

BASE 23:

Pectin	6.2 Gm.
Polysorbate 80	1.0 c.c.
Benzalkonium Chloride	.1 c.c.
Sodium Alginate	.3 Gm.
Stearyl Alcohol	10.4 Gm.
Glycerin	18.0 Gm.
Water or (Ringer's Sol. #1)	64.0 c.c.
To make about	100.0 Gm.

BASE 24:

Pectin	6.2 Gm.
Polysorbate 80	1.0 c.c.
Benzalkonium Chloride	.1 c.c.
Sodium Alginate	.3 Gm.
Stearyl Alcohol	11.4 Gm.
Glycerin	18.0 Gm.
Distilled Water	63.0 c.c.
To make about	100.0 Gm.

BASE 25:

Pectin	7.0	Gm.
Polysorbate 80	1.0	c.c.
Methyl Paraben	.045	Gm.
Propyl Paraben	.025	Gm.
Stearyl Alcohol	6.0	Gm.
Glycerin	17.93	Gm.
Distilled Water	68.0	c.c.
To make about	100.0	Gm.

BASE 26:

Pectin	6.5	Gm.
Polysorbate 80	1.12	c.c.
Methyl Paraben	.05	Gm.
Propyl Paraben	.03	Gm.
Stearyl Alcohol	15.3	Gm.
Glycerin	17.0	Gm.
Water or (Ringer's Sol. #1)	60.0	c.c.
To make about	100.00	Gm.

In compounding Bases 19 to 26 inclusive, the boiling aqueous-alcohol solution was added to the pectin-glycerin mixture as previously described.

Of the series, 19 to 26, the formula for Base 26 yielded a product which had the best appearance, texture and feel. The bases which contained the sodium alginate emitted a disagreeable odor and exhibited a light tan discoloration. Base 26 had a white, glossy surface, which rapidly assumed this appearance after being disturbed. The feel of the base was found to be moist and cooling, with no dryness of "slip", but rather, with a feel characteristic of what might be called a smooth lubricant. A few suspended air bubbles were noticed, but the overall consistency of the base was firm and tenacious, with little flow.

All of the bases of this series were tested for moisture-retainability, according to the previously discussed technique. 30 Gram samples were used and 15 c.c. distilled water was incorporated into each. The weighings were made at successive intervals of 51, 130 and 177 hours. As previously, the weight lost at these intervals was calculated with adjustments for the salts contained in Ringer's Solution, but disregarding the water contained in Benzalkonium Chloride Solution and in the polysorbate. The results are recorded in Table IV.

TABLE IV:

RESULTS OF EVAPORATION TEST OF BASES 19 to 26 USING PECTIN PASTE, N.F. AND HYDROPHILIC OINTMENT, U.S.P. AS CONTROLS.

Preparation	Percent water loss after evaporation 51 hours	130 hours	177 hours
Base 26	12.8	25.3	30.2
" 19	12.9	25.6	30.7
" 20	15.3	28.6	33.4
" 23	14.7	29.8	35.1
" 22	14.8	29.9	36.0
" 25	12.9	30.5	38.3
" 24	14.3	33.3	41.0
" 21	15.0	34.4	43.4
Hydrophilic Ointment, U.S.P.	20.1	38.2	46.3
Pectin Paste, N.F.	17.5	41.4	52.5

A study of the data contained in the submitted tables reveals that in water-retainability, Base 26 surpasses all of the bases tried as well as Hydrophilic Ointment and Pectin Paste.

The elimination of sodium alginate and the addition of more stearyl alcohol improved water-retainability, as may be seen from a study of Bases 15 and 19. Base 15, the best of the sodium alginate series, was however, exceeded in this respect by Base 26. The alcohol content was consequently increased at expense of Ringer's Solution #1, in two trial experiments, with modifications of formula of Base 26. It was, however, found that a further increase in the alcohol content would yield a pasty, unsatisfactory preparation.

A water-absorption test was then tried on the final series, using Pectin Paste, N.F. as the control. Forty-Gram samples of each base were accurately weighed in 100 c.c. beakers, each equipped with a small stirring rod. Distilled water was then added, one c.c. at a time by means of a pipette, and incorporated until a viscous cream that would just flow off the stirring rod without breaking was formed. The results obtained in this test are recorded in Table V.

TABLE V:

WATER ABSORPTION TEST

Preparation (40 Gm.)	c.c. Distilled Water Absorbed
Base 25	20 c.c.
" 21	22 c.c.
" 23	25 c.c.
" 22	26 c.c.
Pectin Paste, N.F.	26 c.c.
Base 24	28 c.c.
" 26	31 c.c.
" 19	35 c.c.
" 20	37 c.c.

Although Bases 19 and 20 showed a somewhat better water-absorption, the excellent ointment-like qualities and water-retainability of Base 26, characterized it as the best all-purpose hydrophilic ointment base developed in this work.

To determine relative stabilities under different conditions, samples of Bases 19 to 26 were placed into clear glass containers equipped with rubber stoppers and stored for eight weeks in a constant temperature oven at 50°C. The results are shown in Table VI.

Similarly, samples of Bases 19 to 26 were stored at 0°C. for nine weeks and at room temperature for ten weeks. The results are also recorded in Table VI.

A study of the data included in Table VI reveals that Base 26, like Pectin Paste, N.F. should be preserved in tight containers away from excessive heat.

Base 11 readily developed mould growths, identified as Cladosporium Herbarum and Aspergillus (sp), with the former predominating.

In a further test for stability, samples of Bases 19 to 26 inclusive, were then placed into half ounce ointment jars and inoculated with moulds obtained from the spontaneous growths which developed in Base 11. Each jar was then capped and examined at different intervals. Hydrophilic Ointment, U.S.P. and Pectin Paste, N.F. were used as controls. The results obtained are shown in Table VII.

TABLE VI:

TEMPERATURE STABILITY TEST

Base	Storage at 50°C. (for 8 weeks)	Storage at 0°C. (for 9 weeks)	Storage at Room Temp. (10 weeks)
19	C-5 L-2	C-2	S
20	C-4 L-1	S	S
21	C-4 L-1	S	S
22	C-4 L-1	S	S
23	C-4 L-1	S	S
24	C-3 L-1	C-1	S
25	C-5 L-2	S	S
26	C-3 L-1	S	S
Hydrophilic Ointment	C-3 B-4	S	S
Pectin Paste	C-3 L-5	M-3	S

M- Mould Growth

L- Liquefaction

B- Bleeding

C- Color Change

S- Stable Throughout Test

Extent
-1 Trace
-2 Slight
-3 Noticeable
-4 Pronounced
-5 Excessive

MOULD TEST, INOCULATIONS WITH CLADOSPORIUM AND ASPERGILLUS (sp)

Base	Preserv./Liq. in 100 Gram.	Time elapsed after inoculation 6 days later	12 days later	22 days later	50 days later	60 days later
19	MP .045 PP .027.65 c.c.	-	M	M	M	M
20	Benzoic Acid .2/62 c.c.	-	-	-	-	-
21	Zeph. Chloride .06/65c.c.	-	-	-	-	-
22	MP .025 PP .015/62c.c.	-	M	M	M	M
23	Zeph. Chloride .1/64 c.c.	-	-	-	D	D
24	Zeph. Chloride .1/63c.c.	-	-	-	-	-
25	MP .045 PP .025/68c.c.	-	-	-	D	D
26	MP .05 PP .03/60c.c.	-	-	-	-	-
Pectin Paste N.F.	Benzoic Acid .2/82.5 c.c.	-	L	L	L	L
Hydrophilic Ointment.U.S.P.	MP .025 PP .015/37 c.c.	-	-	-	-	-

- No Growth
L- Liquefaction
M- Mould Growth
D-Surface discoloration-indicating a very mild growth of mould

A study of the results recorded in Table VII reveals that growth readily developed in Base 22 and that the quantity of parabens used in Base 19 was not adequate to arrest growth. The amount used in the formula of Base 26 was, however, sufficient. Benzalkonium Chloride also proved to be a very efficient preservative. Benzoic Acid was found effective, but produced liquefaction and complete decomposition when added to Pectin Paste.

Comparative costs of Base 26, Pectin Paste, N.F. and Hydrophilic Ointment, U.S.P. were then obtained from a current R. F. Revson Co. price list. The pH of each of the preceding was determined by use of pHydrion papers. These data, with water-absorbability, water-retainability and storage data mentioned previously are recorded in Table VIII.

A study of the data recorded in composite Table VIII reveals that Base 26 has a water-absorbability exceeding that of Pectin Paste, N.F. The water-retainability of Base 26 is shown to exceed that of Pectin Paste, N.F. and Hydrophilic Ointment, U.S.P. which suggests that the base forms a collodion-like surface film capable of retaining moisture. The temperature stability data suggest that Base 26 is superior in this respect to Pectin Paste, N.F.

It was further noted that Base 26 retained its consistency, but underwent a color change from white to tan. Pectin Paste, N.F. and Hydrophilic Ointment, U.S.P. similarly suffered

TABLE VIII

COMPARISON OF PROPERTIES, etc., of BASE 26 WITH THOSE OF PECTIN PASTE, N.F. AND HYDROPHILIC OINTMENT, U.S.P.

Test	Unit, etc.	Time	Hydrophilic Ointment, U.S.P.	Pectin Paste N.F.	Base 26
Water Absorbability	(cc absorbed in 40 Gm. sample)			26 c.c.	31 c.c.
Water Retainability	Per cent water lost from sample	51 hours	21.0 per cent	17.5 percent	12.8 percent
		130 "	28.4 " "	41.5 "	25.6 "
		179 "	46.4 " "	52.5 "	30.2 "
Storage Temperature and Stability	50°C.	8 weeks	C,B	L,C	C
	0°C.	9 weeks	S	M	S
	Room Temperature	10 weeks	S	S	S
Mould Growth	Cladosporium Herbarum and Aspergillus (sp)		S	L *	S
pH	pHydrion papers		7	4	5
Ingredient Cost	1 Kilogram-base		$1.07	$ .63	$1.03

C-Color Change
B-Separation
L-Liquefaction
S-Stable
M-Mould Growth
*-Possible Mould Growth

color changes, but to a somewhat lesser extent. Pectin Paste, N.F., however, underwent liquefaction. Base 26, hence, may be considered as stable at room temperature and at 0°C. That Base 26 may readily be restored after being exposed to water-depleting conditions, was shown by evaporating a 100 Gram sample to a rubbery residue over a steam bath and re-incorporating the water. In performing this test, an amount of water equivalent to that lost was added after softening overnight the mass was rendered homogenous by stirring. This property might well be utilized in making this base available in a more compact water-free form ready to be used whenever necessary by simply blending in the desired quantity of water.

The pH of Base 26 is approximately 5, a factor not detrimental as the pH of the normal skin ranges between 4.2 and 5.6. The cost of ingredients, and the time consumed in preparing the base, are nearly the same as those of Hydrophilic Ointment, U.S.P.

INCORPORATION OF MEDICINAL AGENTS INTO BASE 26

Base 26 was next used in the actual compounding of several official and special ointment formulas.

The procedure followed was to first levigate the medicinal substance with a small portion of the base and then, to similarly incorporate the mixture into the remainder of the base. An appropriate spatula and ointment slab were used, water being occasionally added as a diluent. In the process of compounding, the ingredients were found to blend with the base very easily. This was especially true in the case of balsams, tars, extracts and powders. Difficulty was, however, experienced with Zinc Oxide combinations which solidified on standing, a difficulty corrected by addition of mineral oil and water. The ointments were finally stored at room temperature and at 40°C. for one month, at which time the stabilities were checked. The data thus obtained are recorded in Table IX. Of the thirty-six ointments compounded, only five were found to be unstable. When stored at 40°C. for a like period, seventeen of the thirty-six ointments were found to be unstable.

The release of medicaments from Base 26, as compared to various official ointments, was determined by means of the

TABLE IX:

OINTMENT COMPOUNDING AND STORAGE TEST

Source of Ointment	Usual Content in percent	Ease of Compounding	Appearance & Texture	Room Storage	40°C. Storage
Boric Acid	10	E	E	S	S
Chrysarobin	6	E	E	C	C
Coal Tar	5	E	E	S	H
Mercury Ammoniated	5	E	E	S	C
Penicillin	1000 u/Gm.	E	E	S	S
Sulfur	10	E	E	S	S
Yellow Mercuric Oxide	1	E	E	S	C
Zinc Oxide	20	F	G	S	H,B
N.F. Ointments					
Belladonna	10	E	E	S	S
Benzoic and Salicylic Acid	12 6	E	E	S	H
Calamine	17	F	G	S	H,B

E-excellent F-fair S-stable
G-good P-poor C-color change
H-hardening or crystallization B-separation

TABLE IX: (con't.)

Source of Ointment	Usual Content in percent	Ease of Compounding	Appearance & Texture	Room Storage	40°C. Storage
	5	E	E	S	C
Compound Resorcinol	6 *	F	G	C	H,C
Compound Sulfur	15 *	G	F	B	H,C
Compound Tar	4 *	E	G	C	C,B
Ethyl Amino Benzoate	5	E	E	S	C
Ichthammol	10	E	E	S	S
Iodine	2	E	E	S	S
Mild Mercurous Chloride	30	E	E	S	S
Neo Calamine	15	F	G	S	H,B
Nutgall	20	E	G	S	S
Phenol	2	E	E	S	S
Pine Tar	33	E	E	S	B
Red Mercuric Oxide	10	E	E	S	S
Scarlet Red	5	E	E	S	S
Strong Mercurial	50	E	E	S	B

E-excellent F-fair S-stable
G-good P-poor C-color change
H-hardening or crystallization B-separation
*-usual percent of other medicinal ingredients

TABLE IX: (con't.)

Source of Ointment	Usual Content in Percent	Ease of Compounding	Appearance & Texture	Room Storage	40°C. Storage
Tannic Acid	20	E	E	C	C
SPECIAL					
Alcohol	10	E	E	S	S
Balsam of Peru	10	E	E	S	S
Cod Liver Oil	10	E	E	S	S
Coal Tar Solution	10	E	E	S	S
Menthol	4	E	E	S	S
Methyl Salicylate	10	E	P	S	S
Mineral Oil	10	E	E	S	S
Salicylic Acid	10	E	E	S	S
Sulfathiazole	5	E	E	S	C

E-excellent F-fair S-stable
G-good P-poor C-color change
H-hardening or crystallization B-separation

Food and Drug Administrations' Agar Plate Method.[1] Accordingly, 12-20 c.c. batches of sterile Bacto Nutrient Agar were each inoculated with 0.1 c.c. of a twenty-hour culture of Staphylococcus Aureus and placed in sterile petrie dishes. Inhibition of growth was determined by placing one Gram samples of Base 26 and the official preparation into intimate contact with the surface of the agar. All samples thus prepared were allowed to incubate twenty-four hours before measuring the zones of growth inhibition.

Two one Gram portions of 2 percent Phenol in Hydrophilic Ointment, U.S.P. Penicillin Ointment, U.S.P. and Ammoniated Mercury Ointment, U.S.P. were used as controls in one series of six plates. Respectively, two one gram portions of 2 percent Phenol, 5 percent Ammoniated Mercury, and 1000 units of Penicillin incorporated in Base 26 were placed in another series of six plates.

The diameters of growth inhibition determined in each base are recorded in Table X.

Ointments containing Base 26 were easily removed from the hands and compounding equipment by use of warm water and a test tube brush. Smears on clothing similarly treated, left no stain.

---

1. Ernest Carr McCulloch; Disinfection and Sterilization; 2nd. Edition, Publishers, Lea & Febriger; Pg. 193.

TABLE X:

GROWTH INHIBITION TEST

Ointment	Diameter of the Inhibition Area After 24 hours of contact Sample I	Sample II
Base 26 with 2 percent Phenol	9 mm	11 mm
Hydrophilic Ointment, U.S.P. with 2 percent Phenol	6 mm	7 mm
5 percent Ammoniated Mercury in Base 26	12 mm	14 mm
Ammoniated Mercury, U.S.P.	5 mm	5 mm
1000 u/Penicillin in Base 26*	9 mm	10 mm
Penicillin Ointment, U.S.P. 1000 u/Gm. (Lilly's)	13 mm	14 mm

* Prepared 6 weeks prior to test.

CONCLUSIONS

1. An improved pectin ointment base has been developed.
2. Various properties and incompatibilities of the base have been determined.

BIBLIOGRAPHY

1. Fantus, Bernard and H. A. Dyniewicz. Pastes 1. For Dermatologic Use. J. A.Ph.A. Vol. 28. Pg. 548. Aug. 1942.

2. Goldner, Karl J. Medical and Pharmaceutical Applications of Pectin. Am. J. of Pharmacy. Vol. 114. Pg. 41-6.

3. Goldner, Karl J. Pectin Emulsions and Ointments. Pract. Edition, J. A.Ph.A. Vol. 13. Pg. 324-26. Sept. 1942.

4. Kertesz, Z. I. The Pectinic Substances. Interscience Publishers, Inc. New York. Pg. 5. 1951.

5. Maclay, W. D., Alland Shepherd and Harry Lotzkar. Use of Pectin in Pharmaceutical Pastes and Ointments. Scientific Edition, A.Ph.A. Vol. 33. Pg. 113-118. April, 1944.

6. Maier, Eugene. Preservation of Biological Fluids with Alkyl-Dimethyl Benzyl Ammonium Chloride. J. Bacteriology 38. Pg. 33. 1939. July-Dec.

7. McCulloch, Ernest Carr. Disinfection and Sterilization. 2nd. Edition. Publishers, Lea & Febriger, Pg. 193.

8. The pH of Ointments. Pract. Edition, J. A.Ph.A. Vol. 3. Pg. 340. Oct. 1942.

9. Universal Hydrophilic Ointment Base. J. A.Ph.A. Pract. Edition. Pg. 475. 1951.